REMARKS

Claims 1-11, 14-19 and 21 are currently pending in this application. Claims 1 and 2 have been amended. Claims 12 and 13 have been canceled. Claims 10, 19, and 21 have been withdrawn as the result of a restriction requirement. No new matter has been added. Reconsideration is respectfully requested in view of the above amendments and the following remarks.

Applicants' Response to §112, Second Paragraph Rejection

Claims 3-6 and 13-15 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Examiner states that a broad range or limitation, together with a narrow range or limitation, that falls within the broad range or limitation, is considered indefinite. In particular, the Examiner states that claims 3-6 recite broad ranges of amounts of ingredients and also "preferably" followed by narrower ranges. Applicants submit that the claim language objected to by the Examiner was removed from the claims in a preliminary amendment accompanying the original application submitted on March 11, 2005. In the preliminary amendment, claims 3-6 and 13-15 were amended to remove the language objected to by the Examiner. The listing of claims included in the present amendment reflects the current version of the claims including the amendments made in the preliminary amendment. Therefore, Applicants respectfully submit that the Section 112 rejection should be withdrawn.

Applicants' Response to §103 Rejections

Claims 1-9 and 11-18 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over WO 0016775 (hereinafter, "the '775 publication") in view of the journal article to Jumaa et al. entitled "Parental emulsions stabilized with a mixture of phospholipids and PEG-660-12-hydroxystearate: evaluation of accelerated and long-term stability" (hereinafter "Jumaa"). Applicants respectfully request reconsideration on the basis that the cited combination fails to suggest Applicants' claims, as amended herein.

The Examiner contends that the '775 publication generally discloses:

> a pharmaceutically acceptable topical formulation comprising pryidone together with an excipient, characterized in that the excipient comprises one or more plasticizers, one or more antioxidants, one or more gel-forming agents and a pH adjusting agent.

(Office Action, at page 4).

The Examiner acknowledges that the '775 publication does not expressly disclose macrogol 15 HS (i.e., a surface-active solubilizer), the elected solvent (i.e., maize oil), and the elected medium-chain triglyceride (i.e., caprylic/capric triglyceride) as ingredients in the preparation. For such disclosure, however, the Examiner points to Jumaa. The Examiner alleges that "Comparative Example 2 recited in '775 combined with Jumaa et al. discloses the limitations of claims 1-17, which are generic to claim 18." (Office action, at page 5). According to the Examiner, "it would have been obvious to a person of ordinary skill in the art to make the claimed invention by picking and choosing well-known excipients commonly used in topical preparations." (Office Action, at page 5). The Examiner concludes that it would have been obvious to combine the teachings of the '775 publication with Jumaa to obtain the invention recited in Applicants' claims.

Applicants have amended claim 1 herein to further define the invention. The '775 publication and Jumaa fail to disclose or suggest Applicants' claims, as amended herein. More specifically, the present application refers to a pharmaceutical cream preparation in the form of an oil-in-water (o/w) emulsion wherein the lipophilic phase includes as active ingredients an optionally substituted 1-phenyl-2-(1H)-pyridone compound or a pharmaceutically acceptable salt thereof, preferably the compound pirfenidone. Oil-in-water (o/w) emulsions containing pirfenidone are intrinsically unstable, as explained in the introduction of the present application (see e.g. paragraph [0007] of U.S. Patent Publication No. 2006/0039931 A1).

The present application also noted that: "Phospholipids, e.g. lecithin, are unsuitable as surface-active solubilizers or as emulsifiers within the framework of the present invention." (see paragraph [0042] of U.S. Patent Publication No. 2006/0039931 A1, last sentence). The present invention therefore specifically excludes phospholipids from being used as a component in the claimed oil-in-water (o/w) emulsion, as recited in Applicants' amended claim 1 ("said preparation being substantially free of phospholipids").

The '775 publication refers to a topical formulation, preferably containing pirfenidone as the pharmaceutically active compound. The '775 publication discloses gels for topical use, and describes the use of gel-forming agents for obtaining stable gels. Oil-in-water (o/w) emulsions are not mentioned. The '775 publication does not contain any indication how stable oil-in-water (o/w) emulsions containing pirfenidone could be made.

Jumaa describes their investigation with reference to different emulsion formulations stabilized with a mixture of phospholipids and PEG-660-12-hydroxy-starate (Solutol HS15). Phospholipids are known to stabilize lipid emulsions. However, phospholipids are sensitive to pH changes. Jumaa therefore investigates the combination of phospholipids together with Solutol HS15 in order to find out whether or not such a combination gives more stable emulsion formulations than phospholipids alone. A phospholipid is always present. The present invention, as recited in amended claim 1, to the contrary, specifically excludes phospholipids from being used as a component.

Further, Jumaa refers to different emulsion formulations in general, because oil-in-water (o/w) emulsions per se are intrinsically unstable (see Jumaa, Introduction). Pirfenidone itself is known to destabilize emulsions; but Jumaa does not refer to emulsions containing pirfenidone.

Jumaa therefore (i.e., always using a phospholipid and not referring to pirfenidone at all) cannot give any indication how to solve the problem of producing a stable oil-in-water emulsion not containing any phospholipids and in addition at the same time containing pirfenidone as an active ingredient.

Therefore, Jumaa is not relevant and even points away from the present invention. In this sense, Jumaa cannot be combined with the cited '775 publication in rejecting Applicants' amended claims.

In view of the above, claims 1-9 and 11-18 are patentable over the '775 publication in combination with Jumaa. Applicants respectfully request reconsideration of the Section 103 rejection over this cited combination.

Applicants' Response to Double Patenting Rejection

Claims 1-9 and 11-18 are rejected on the grounds of non-statutory obviousness-type double patenting as allegedly being unpatentable over claims 1-3, 5, and 7-10 of U.S. Patent No. 6,492,395 to Scheiwe et al. (hereinafter "Scheiwe") in view of Jumaa. The Scheiwe patent is the U.S. equivalent of the '775 publication, discussed in detail above. In particular, both are based on International Application No. PCT/EP98/05971. Accordingly, Applicants' remarks regarding the patentability of the present claims over the '775 publication in view of Jumaa are equally applicable herein. Applicants, therefore, respectfully submit that claims 1-9 and 11-18 are patentable over Scheiwe in view of Jumaa. Applicants respectfully request reconsideration and withdrawal of the obviousness-type double patenting rejection.

Favorable action is earnestly solicited. Should the Examiner have any questions or comments concerning the above, the Examiner is respectfully invited to contact the undersigned attorney at the telephone number given below.

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